REMARKS

Claims 1 and 3-33 are pending. No claims have been cancelled, added or amended herein.

It is noted that the previous rejections of claim 20 under 35 U.S.C. § 103(a) as unpatentable over Davies (US2005/0152846) in view of Clarke (US2002/0103260) and of claims 1, 7-10, 13-16, 21, 23-25, 27, 28 and 32 as unpatentable overUS20020103260 ("Clarke"), in view of WO 92/18110 ("Trofast I") and WO 01/89491 ("Trofast II"), have been withdrawn.

It is further noted that Applicant's declaration filed November 22, 2010 was deemed by the Examiner to provide support for the upper range of water content recited in claim 1.

Rejection under 35 U.S.C. §§ 103(a)/101

Claim 20 remains provisionally rejected as claiming the same invention as claim 20 of co-pending application USSN 10/574,302. Applicant will address this rejection at such time as one of the conflicting claims is deemed allowable.

Rejections under 35 U.S.C. § 103(a)

1. Claim 20: Blondino in view of Clarke

Claim 20 is newly rejected under 35 U.S.C. § 103(a) as unpatentable over Blondino (US 6,451,285) in view of Clarke (US2002/0103260). The rejection is traversed.

Claim 20 is directed to a pharmaceutical aerosol formulation for use in a metered dose inhaler (MDI) consisting essentially of formoterol fumarate dihydrate in suspension, a propellant and ethanol, wherein the moisture content of the formulation is in the range of from 50 ppm to 800 ppm.

Blondino is relied upon for allegedly describing a suspension aerosol formulation containing formoterol fumarate and having a moisture content of about 429 ppm, which is within the claimed range. Office action at p.4-5 (bridging paragraph) (pointing to Example 10 of Blondino). Clarke is relied upon for describing an aerosol composition for a metered dose inhaler comprising formoterol fumarate in the dihydrate form. Office action at p. 5.

Neither Blondino nor Clarke, nor their combination, provides the skilled person with the necessary direction to make the claimed formulations consisting essentially of formoterol fumarate dihydrate in suspension with a reasonable expectation of success. Both Blondino and Clarke are silent with regard to how to obtain a formulation consisting essentially of the

dihydrate. Indeed, absent Applicants' discovery that formoterol fumarate stabilizes into the di-hydrate form at the specified water content, the skilled person could not have expected success in obtaining a formulation consisting essentially of the dihydrate.

The Examiner's construction of "consisting essentially of" in the claims to be equivalent to "comprising" is based upon the alleged absence of "a clear indication in the specification or claims of what the basic and novel characteristics actually are." Office Action at p. 5. However, Applicants have made clear on this record that the invention lies in the ability to obtain a stable formulation consisting predominantly of the dihydrate form by controlling the water content of the formulation, as evidenced by the data presented in two declarations by Dr. Rudi Mueller-Walz along with the responses filed on February 26, 2010 and November 22, 2010. As discussed in those declarations, Applicant found that at certain water contents formoterol fumarate exists as an unstable mixture of the anhydrate and dihydrate forms. Applicant further found that by controlling the water content as specified in the claims, it was possible to obtain a stable formulation containing predominantly the dihydrate form. This is further described by the specification as the basic and novel characteristic of the claimed invention. For example, the specification teaches that the Applicant has found a novel means of stabilizing a suspension formulation of formoterol fumarate dihydrate by presenting it in a form having a particularly low water content, that is of about 4.8 to 4.288%, and more preferably 4.5 to 4.28%. Specification at p. 3, lines 9-22. Accordingly, it is inappropriate for the Examiner to construe "consisting essentially of" as "comprising" when it is clear from the specification and the record that the dihydrate form is a basic and novel characteristic of the claimed formulations.

2. Clarke, alone and in combination with either Kordikowski or Keller

Claims 1, 7, 10, 13-17, 21, 23-24, 27, 28 and 32 are newly rejected under 35 U.S.C. § 103(a) as unpatentable over Clarke alone; claims 3-6, 21, 22, 26, and 33 are rejected over Clarke in view of U.S. Pub. No. 2003/0223939 ("Kordikowski"); and claims 8, 9, 11, 12, 18, 19, 25, and 29-31 are rejected over Clarke in view of U.S. 6,475,467 ("Keller").

Claim 1 is directed to a pharmaceutical aerosol formulation for use in a metered dose inhaler (MDI) consisting essentially of formoterol fumarate di-hydrate in suspension, a propellant and ethanol, wherein the formoterol fumarate di-hydrate has a water content of 4.8 to 4.28% by weight, and a steroid in suspension. The remaining claims depend, directly or indirectly, from claim 1.

The Examiner relies on Clarke for describing an aerosol composition for a metered dose inhaler comprising formoterol fumarate dihydrate (FFDH), ethanol, a propellant (HFA 134a), and a steroid (fluticasone propionate) (see Example 1 of Clarke). Applicant notes that Clarke describes only one aerosol formulation while describing 215 dry powder formulations of FFDH and fluticasone. Applicant further notes that Clarke is silent as to the water content of the single exemplified aerosol formulation. Nor does Clarke provide any guidance regarding what the water content of an aerosol formulation of FFDH should be.

Regarding the description of the dihydrate form, the Examiner relies on the statement in Clarke that the formoterol fumarate "may be present in a particular crystalline form" such as the dihydrate form. Clarke at para. 10. Clarke does not describe how to obtain a formulation having formoterol fumarate in a "particular" crystalline form, much less the dihydrate form. Clarke refers to WO 95/05805 for the fact that formoterol fumarate "may be present in a particular crystalline form." *Id.* U.S. Patent No. 5,709,884 is the U.S. national phase entry of WO 95/05805 ("the '884 patent", of record as reference "A" in IDS filed October 7, 2009). But the '884 patent does not specify the water content of its formulations. And the presence of the dihydrate form is predicted based on an indirect measurement, the amount of heat released during recrystallization. *See* the '884 patent at col. 6, lines 36-41. Accordingly, even taking into account the description of WO 95/05805 (as evidenced by its US national phase entry, issued as the '884 patent), the skilled person would have failed to find any clear and unambiguous suggestion to control the water content as recited in Applicant's claims in order to arrive at a composition consisting essentially of the dihydrate form. Thus, neither Clarke, nor the reference cited by Clarke for the proposition that formoterol fumarate may be present in a particular crystalline form, such as the dihydrate form (*i.e.*, WO 95/05805), would predictably lead one to a composition consisting essentially of formoterol fumarate dihydrate in suspension, a propellant and ethanol, wherein the formoterol fumarate dihydrate has a water content of 4.8 to 4.28% by weight, and a steroid in suspension, as required by claim 1.

Applicant submits that the Examiner's construction of the claim term "consisting essentially of" to mean "comprising" is in error, for the reasons discussed above in relation to the rejection of claim 20.

In summary, a *prima facie* case has not been established with respect to claim 1, or its dependent claims, because the cited reference fails to describe or suggest each and every element of the claimed invention. In particular, Clarke fails to describe or suggest a formulation consisting essentially of formoterol fumarate dihydrate and containing the water content

specified in the claim. Moreover, Clarke does not provide the clear direction or guidance necessary to obtain the claimed compositions consisting essentially of the dihydrate form with a reasonable expectation of success because Clarke is silent with regard to how to obtain a composition that is predominantly in the dihydrate form. For all of these reasons, reconsideration and withdrawal of the rejection as applied to claim 1, and its dependent claims, is requested.

Claim 17

Claim 17 depends from claim 1 and specifies that the ethanol is present in amounts of less than 2.5% by weight (emphasis added). Applicant's specification teaches that one of the advantageous aspects of the claimed formulations is to allow the use of very small amounts of ethanol. *See e.g.*, the specification at p. 3, lines 9-16 and at p. 12, lines 4-11. It is noted that the Examiner rejects claim 17 on the basis of the description of Example 1 in Clarke, which describes ethanol at 2.5%. *See* Clarke at para. 24. But Clarke does not describe or suggest the use of ethanol in amounts less than 2.5%, as required by claim 17. Accordingly, a *prima facie* case of obviousness has not been established with respect to claim 17 for all of the reasons discussed above in relation to claim 1, and for the additional reason that Clarke does not describe or suggest the ethanol content recited in claim 17. Reconsideration and withdrawal of the rejection as applied to claim 17 is requested.

Claims 3-6, 21, 22, 26, and 33

The Examiner cites Kordikowski for describing certain aspects of dependent claims 3-6, 21, 22, 26, and 33. Office Action at pp. 8-10. However, Kordikowski fails to render obvious the subject matter of the rejected claims because it does not remedy the deficiencies of Clarke, as discussed above. Accordingly, Applicant requests reconsideration and withdrawal of the rejection as applied to claims 3-6, 21, 22, 26, and 33.

Claims 11, 12, 18, 19, and 29-31

The Examiner cites Keller for its teachings relating to the subject matter of dependent claims 11, 12, 18, 19, and 29-31. Office Action at p. 10-14. However, Keller fails to render obvious the subject matter of the rejected claims because Keller does not remedy the deficiencies of Clarke, as discussed above.

Double Patent Rejection

Claims 1, 3-19, and 21-33 are provisionally rejected on grounds of nonstatutory obviousness-type double patenting as unpatentable over claims 1, 3-19, and 21-33 of co-pending application USSN 10/574,302 in view of Clarke. It is noted that this is a provisional rejection. Applicant will address this rejection at such time as at least one of the rejected claims is deemed allowable.

Applicant submits that the application is in condition for allowance and request an action for same. Please charge any additional fees that may be due, or credit any overpayment, to Deposit Account No. 50-0311, Reference No. **28069-624N01,** Customer Number: **35437**.

Respectfully submitted,

/Muriel Liberto/

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